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October 27, 1992

Document Processing Center (TS-790)
Office of Toxic Substances
U.S. Environmental Protection Agency
401 M St., S.W.
Washington, D.C. 20460

Attn: Section 8(e) Coordinator (CAP Agreement)

RE: Report Submitted Pursuant to the TSCA Section 8(e) Compliance Audit Program

[ ]

Dear Sir/Madam:

This letter and the enclosed study report contain Confidential Business Information. All information enclosed in brackets [] is claimed trade secret and confidential.

[ ] This information is not owned by [ ] and was obtained during pre-licensing discussions with a foreign company who, to our knowledge, is not subject to TSCA reporting requirements.

The submission involves summary information on a dose range-finding teratogenicity study in rats, dose range-finding reproduction study in rats and ecotoxicity results for a variety of freshwater species on [ ], the material can be generically referred to as an alkyl and aryl substituted organotin compound.

In the range-finding rat teratology study fetotoxicity, reduced fetal weights and ossification abnormalities were noted at dosages of 100, 300 and 1000 mg/kg. These effects were accompanied by severe maternal toxicity which resulted in the deaths of several animals in these groups.

In the range-finding rat reproduction study the number of uterine implants and litter size were reduced at 400 ppm. Pup weights on day 14 of lactation were reduced at 200 and 400 ppm. Parental animals of both sexes exhibited marked reductions in food intake and bodyweight gain during the pre-mating period through termination of the study.

2/9/93

The 48-hour LC 50 values to three fish species, including carp and trout, varied between 0.007 and 0.011 ppm. Other aquatic species including a frog had LC 50 values of 0.04 - 0.05 ppm.

Further questions regarding this submission may be directed to me at [ ].

Sincerely,

[ ]

Enclosures

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Teratogenicity study in rats with [ ]

A preliminary study

June 10, 1988

Study Director: [ ]

[ ]

Summary

A preliminary study was conducted to select proper dose levels prior to initiation of a teratogenicity study in rats with [ ] The test substance was suspended in 1% aqueous solution of carboxymethylcellulose and administered orally to Crj : CD (SD) rats, 7 per group, at doses of 0, 30, 100, 300, and 1000 mg/kg/day from day 6 to day 15 of gestation.

With respect to the maternal rats, adverse effects of the test substance were observed in all treated groups. In the clinical observations, loose stool and/or diarrhea were found in 2 dams in the 30 mg/kg group during the period of administration. In the higher dose groups, these findings were observed in all maternal animals, and 4, 5, and 7 dams in the 100, 300, and 1000 mg/kg groups, respectively, died of digestive-system disorders during days 11 (6th day of administration) to 18 (3 days after completion of administration) of gestation. Mean body weights, body weight gains, and food consumption of the survived dams were extremely lowered with increasing dose levels.

With respect to the fetuses, no adverse effect was found in the 30 mg/kg group. However, fetal weights of both sexes in the 100 mg/kg group were slightly lower than those in the control group. In addition, a significantly higher incidence of fetal resorptions and deaths and a decrease in the number of live fetuses were observed in the 300 mg/kg group.

Teratological examination of fetuses revealed significant increases in the incidences of splitting of the thoracic

vertebral bodies and thymic remnant in the neck, which were classified as a skeletal malformation and a visceral variation, respectively, in the 100 mg/kg group in which more than half of the dams died. These alterations were considered not to be caused by the primary effect of the test substance on the developing fetuses but related to growth reterdation of fetuses which was attributed to the severe toxicity toward maternal animals.

Based on these results, a dose level of 30 mg/kg/day or less is recommended as the high dose level in the definitive teratogenicity study.

Reproduction Study in Rats with [redacted]

Preliminary Study

Study Number [redacted]

January 24, 1990

[redacted]

Summary

A preliminary study was conducted to select proper dose levels prior to initiation of a two-generation reproduction study in rats with [ ] The test substance was incorporated into the basal feed and administered orally to CD(SD) rats, 8 males and 8 females per group, at doses of 0, 20, 100, 200, and 400 ppm during the 5-week pre-mating-growth and subsequent breeding periods to evaluate the potential effects of the test substance on reproductive performance of parental animals and growth of their offspring.

With respect to the parental animals, no adverse effects were observed in the 20 and 100 ppm groups. Although the male body weights in these groups were slightly lower than those in the control group throughout the treatment period, the differences between the treated and control groups were not statistically significant. In the 200 ppm group, on the other hand, body weights and food consumption of both males and females were significantly lowered through the most part of the treatment period. Significantly decreased values in these parameters were consistently found in the 400 ppm group throughout the entire treatment period.

With respect to the reproductive performance, no treatment-related adverse effects were observed in any parameters in the 20, 100, and 200 ppm groups. In the 400 ppm group, however, group mean number of implants and pups delivered were significantly lower than those in the control group.

With respect to the offspring, no treatment-related adverse effects were observed in the 20 and 100 ppm groups. In the 200 ppm group, significantly decreased pup weights were found on day 14 of lactation and thereafter. The values in the 400 ppm group were significantly decreased on day 4 of lactation and thereafter.

Based on these results, it is concluded that dose levels of 100, 200, and 400 ppm correspond to the no-observed-effect level, minimum toxic level, and sure toxic level, respectively, for both parental animals and their offspring. As to the effects on reproductive performance, on the other hand, 400 ppm is considered to be the minimum toxic level. Thus, dose levels of 200 ppm and 20 ppm or less are recommended for the high dose level and low dose level, respectively, in the definitive reproduction study.

Study Director

[redacted]

NON-TARGET ORGANS

on-target organism

. Acute Wildlife tox

ORGANISM		Technical (ppm)	Formulation (a.i.ppm)
Cyprinus carpio	48 hrs LC_{50}	0.0072	0.0077
Oryzias latipes	48 hrs LC_{50}	0.0115	0.0372
Salmo gairdneri	48 hrs LC_{50}	0.00988	
Daphnia pulex	3 hrs immobili.	3.43	4.99
Monia macrocopa	3 hrs immobili.	1.67	6.86
Sinotaia quadrata	96 hrs LD_{100}	0.0508	0.0891
Procambarus clakii	48 hrs LD_{100}	0.0432	0.177
Rana limnocharis	96 hrs LD_{100}	0.0522	0.124
Eisenia foetida			
paper filter	72 hrs LD_{100}	0.0003mg/cm^2	
artificial soil	14 days LD_{100}	488mg/kg	

Prolonged Toxicity Test

(14-Day Semi-static test)

) Killfish(Orizias latipes)

LC50 VALUES FOR EACH OBSERVATION DAY (mg/L)

)ays after :reatment	1 day	2	3	4	5	6	7
	0.0121	0.0113	0.0107	0.0101	0.0095	0.00983	0.00983
)ays after :reatment	8 day	9	10	11	12	13	14
	0.00983	0.00983	0.00973	0.00943	0.00933	0.00923	0.00914

Triage of 8(e) Submissions

Date sent to triage: 12/8/95

NON-CAP CAP

Submission number: 12708A

TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX CTOX EPI RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

For Contractor Use Only

entire document: 0 1 2 **pages** 1,2 **pages** 1,2,4,5

Notes:

Contractor reviewer : _____ **Date:** 3/14/95

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 1092 - 12708 (5) SEQ. A

TYPE: (INT) SUPP FLWP

SUBMITTER NAME: Confidential

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0675) REFER TO CHEMICAL SCREENING
(0676) CAP NOTICE

VOLUNTARY ACTIONS:
0401 NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKERS/OTHERS
0404 LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP/USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 10/27/92 OTS DATE: 10/30/92 CSRAD DATE: 02/09/95

CHEMICAL NAME: Organotin, alkyl and aryl substituted

CAS#: Confident

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
(0207)	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
0209	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
0212	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
(0220)	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE REQEST DELAY	01 02 04
(0224)	PROD/COMP/CHEM ID	01 02 04
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
0228	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
0243	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
0248	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

RTDX

TRIAGE DATA:	NON-CBI INVENTORY	ONGOING REVIEW	SPECIES	TOXICOLOGICAL CONCERN:	USE:	PRODUCTION:
	YES	YES (DROP/REFER)	(RAT)	LOW		
CAS SR	NO	NO (CONTINUE)	Fish frog	(MED)		
	(IN TRIAGE)	REFER		HIGH		

COMMENTS: Devel + Repro (range finding)

DEVELOP
1000 mg/kg - 7/7 dams died
300 mg/kg - 5/7 dams died - increased fetal resorptions + deaths
100 mg/kg - 4/7 " " fetal weights reduced, skeletal malformation + cervical variation
30 mg/kg - diarrhea, reduced body wt + food consumption; no adverse effects on fetuses

Reproduction
1500 ppm - dec BW + food consumption of parents reduced # implants + litter size; reduced # of offspring
600 ppm - some effect on parents reduced # offspring wt
120+1000 ppm - NO effects